



ACM Global - Central Laboratory

**STUDY AC-060A202: CONTROL
Uwe Althauser**



ACM Project Team - Europe

ACM Global Central Laboratory, York, UK

Stacey Fergusson Global Project Manager
Zoe Denham Deputy Project Manager

Telephone: +44 1904 699400 Fax: +44 1904 699401
Investigator@acmgloballab.co.uk

Laboratory hours: Monday - Friday 8am-5pm GMT
Saturday 8am-12pm GMT

Out of office hours calls are diverted to the on
call project manager



AC-060A202: CONTROL – Central Laboratories
Investigators Meeting, Barcelona – 20 & 21 January 2011

ACM Services for AC-060A202

- Laboratory testing and Specimen Storage
- Provision of Laboratory kits
- Sample Collection & processing instructions
- Sample shipping logistics
- Data Resolution
- Result Reporting



AC-060A202: CONTROL – Central Laboratories
Investigators Meeting, Barcelona – 20 & 21 January 2011

Visit Schedule

Test	Screening		Treatment						Run-out EOS Visit 8 Week 14	Unscheduled
	Visit 1 Week -2	Randomisation Visit 2 Day 1	Visit 3 Week 1	Visit 4 Week 2	Visit 5 Week 4	Visit 6 Week 8	EOT Visit 7 Week 12			
	+ -4/+ 2 days	-	+3/-1 days	+3/-1 days	+3/-1 days	±3 days	±3 days	+3/-1 days		
Haematology RBC count, haemoglobin, haematocrit, platelet count, WBC total & absolute differential: basophils, eosinophils lymphocytes, monocytes, neutrophils and percentage eosinophils and basophils	X	X	X	X	X	X	X	X	X ⁶	
Clinical Chemistry Sodium, potassium, chloride, calcium, urea, creatinine, AST, ALT, ALP, Total bilirubin, direct bilirubin, LDH, total cholesterol, triglycerides, fasting glucose, total protein, albumin, uric acid, C-reactive protein	X	X	X	X	X	X	X	X		
TSH, Total T3, total T4		X						X		
Total IgE		X	X	X	X	X	X	X	X	
Serum Pregnancy Test	X		X	X	X	X	X	X	X	
Urinalysis	X	X	X	X	X	X	X	X	X	
Urine Pregnancy Test²		X ²								X
RAST⁷ Standard panel of 12 allergens tested - Specific IgE	X							X		
PK sampling^{4,3}			X	X	X	X	X	X		X
PK sampling fasted^{5,3}				X						
PK sampling fed^{5,3}					X					
PD-1 IL-4, IL-5, IL-13		X	X	X	X	X	X	X	X	X
CRTH2 mRNA levels (PD-2)		X						X		
CRTH2 SNPs analysis (PD-3)		X								

Visit Schedule

Notes

- Standard Regional RAST allergen panels will be tested. The Investigator will have the opportunity to choose up to an additional 2 allergens to be tested, from a list provided in Central Laboratory Investigator Instruction Manual.
- All PK Samples must be protected from light by using the amber plasma transport tubes provided in the laboratory kit.



AC-060A202: CONTROL – Central Laboratories
Investigators Meeting, Barcelona – 20 & 21 January 2011

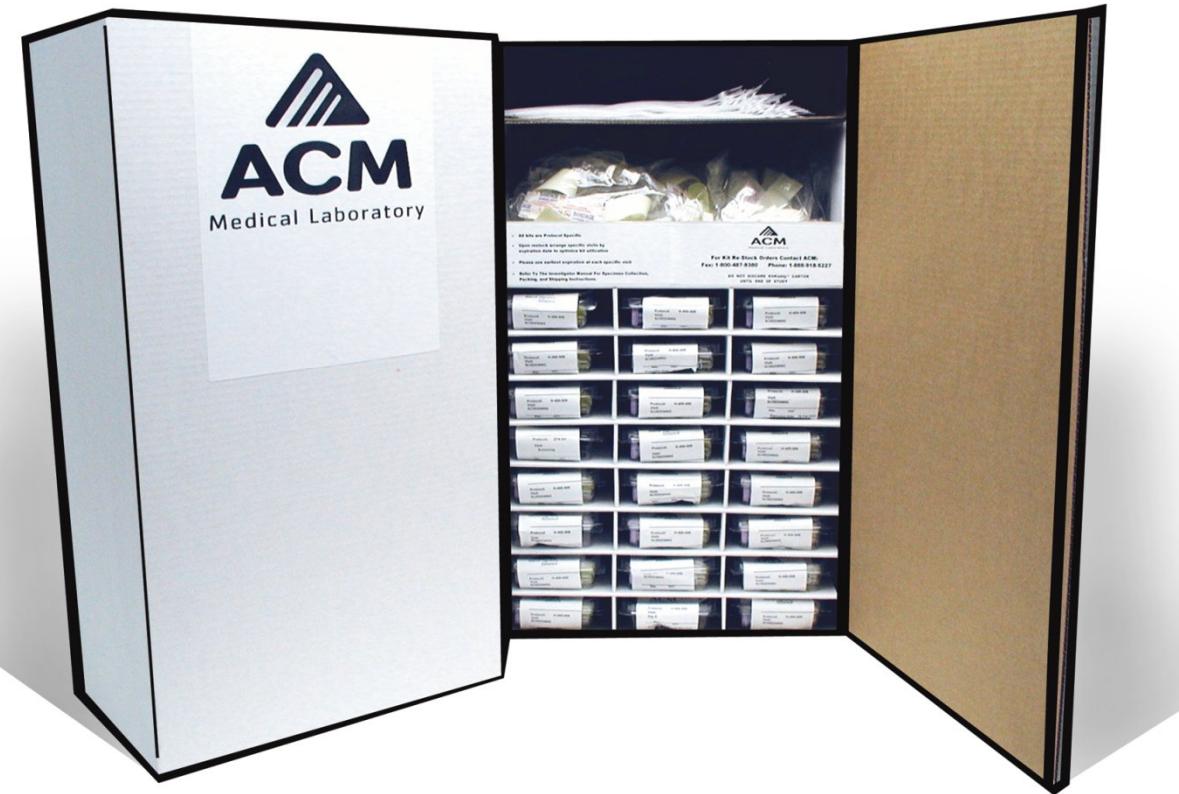
Laboratory Supplies – Kits

- Initial supplies shipped in ACM KitKaddy – 1 per site
- Laboratory kits for AC-060A202 are supplied in transparent plastic trays contained within KitKaddy
- Laboratory kits are visit specific and contain all draw tubes required at the defined visit
- All documentation for sample handling and shipping is supplied
- Additional supplies provided in bulk alongside KitKaddy



AC-060A202: CONTROL – Central Laboratories
Investigators Meeting, Barcelona – 20 & 21 January 2011

Laboratory Supplies – KitKaddy



AC-060A202: CONTROL – Central Laboratories
Investigators Meeting, Barcelona – 20 & 21 January 2011

Laboratory Supplies – Additional Supplies

- Laboratory manual
- Sample processing instructions for lab bench
- Aliquot storage boxes for -20°C freezer
- Urine pregnancy test kits and instructions
- Urinalysis dipstick kit and instructions
- Spare tubes and labels
- Flat-packed sample transport boxes
- Pre-printed courier documentation and flyer bags



AC-060A202: CONTROL – Central Laboratories
Investigators Meeting, Barcelona – 20 & 21 January 2011

Laboratory Supplies – Re-supply

- Initial supply will be provided to all sites, sites are then responsible for monitoring kit levels
- For resupply e-mail

investigator@acmgloballab.co.uk

- State protocol number AC-060A202
- Number & type of kits and/or additional supplies required
- Latest date required on site
- Supplies are dispatched within 7 working days of receipt of order



AC-060A202: CONTROL – Central Laboratories
Investigators Meeting, Barcelona – 20 & 21 January 2011

Laboratory Manual

- Study Contact Information
- Laboratory supplies – contents, re-supply
- Laboratory Testing Schedule
- Request form and sample label completion
- Sample Collection & Handling
- Packaging & Shipping Instructions
- Laboratory Accreditations and Certifications



AC-060A202: CONTROL – Central Laboratories
Investigators Meeting, Barcelona – 20 & 21 January 2011

Request Form

- Note there are visit specific request forms
- Fill in prior to sample collection
- Carefully complete all requested patient demographic details
- Ensure correct study visit is indicated by using the tick boxes



AC-060A202: CONTROL – Central Laboratories
Investigators Meeting, Barcelona – 20 & 21 January 2011

Request Form (2)

➤ Complete:

- Subject ID – 5 digits
- Age at Screening – 2 digits (years)
- Sex: M/F
- Sample Draw Date: DD/MMM/YYYY
- Sample Draw Time: HH:MM (24 hr clock) – Safety and PD-1 where applicable
- Name of person completing form
- Choice of 2 additional allergens on RAST request form – fill in by hand at Visit 1 only

**Clinical Trial Request Form
Actelion Pharmaceuticals Trial: AC-060A202
(063/005 and 063/005F)**

Subject Number	<input type="text" value="1"/> <input type="text" value="2"/> <input type="text" value="3"/> <input type="text" value="4"/> <input type="text" value="5"/>	Sex: <input type="text" value="F"/>					
Age at Screening	<input type="text" value="2"/> <input type="text" value="5"/>	Years					
Initials	<input type="text" value="X"/> <input type="text" value="X"/> <input type="text" value="X"/>						
Sample Date:	<input type="text" value="0"/> <input type="text" value="1"/> <input type="text" value="0"/> <input type="text" value="C"/> <input type="text" value="T"/> <input type="text" value="2"/> <input type="text" value="0"/> <input type="text" value="1"/> <input type="text" value="0"/>	<small>d d m m m y y y y</small>					
Safety Sample Draw time:	<input type="text" value="0"/> <input type="text" value="8"/>	<small>h h</small>	<input type="text" value="4"/> <input type="text" value="5"/>	<small>m m</small>			
PD-1 Sample Draw time:	<input type="text" value="0"/> <input type="text" value="8"/>	<small>h h</small>	<input type="text" value="5"/> <input type="text" value="5"/>	<small>m m</small>			
Investigator Name:	Dr Investigator	Site No:	1	2	3	4	
Completed by:	<u>S. Ferguson</u>						
Kit C Visit 3, 4, 5, 6							
Please tick as appropriate:							
<input checked="" type="checkbox"/> Tick box to confirm that patient is fasting							
<input checked="" type="checkbox"/> Visit 3 Week 1							
<input type="checkbox"/> Visit 4 Week 2							
<input type="checkbox"/> Visit 5 Week 4							
<input type="checkbox"/> Visit 6 Week 8							
Is pregnancy test required? Yes <input type="checkbox"/> No <input checked="" type="checkbox"/>							
PLEASE REFER TO INSTRUCTIONS PROVIDED FOR COLLECTION AND DISPATCH OF SAMPLES							
<small>FOR LAB USE ONLY</small>							
Ambient: 2 x S, 1 x E							
Frozen: 1 x P (PK), 1 x S (PD)							
Final Version 15/09/2010							
AC-060A202: CONTROL – Central Laboratories Investigators Meeting, Barcelona – 20 & 21 January 2011							

For lab use

V3, V3PD, V3PK
V4, V4PD, V4PK
V5, V5PD, V5PK
V6, V6PD, V6PK
SPT?

Request Form (3)

- Indicate using tick box
 - Visit
 - Fasting status
 - Pregnancy testing requirement
- Pre-printed information
 - Investigator name
 - Site number
 - Initials - XXX
- Complete tube labels
 - Ensure information is consistent with request form
- Adhere a completed label to all tubes – Unlabelled tubes will not be processed or analysed



AC-060A202: CONTROL – Central Laboratories
Investigators Meeting, Barcelona – 20 & 21 January 2011

Sample Collection-General Guidelines

- Practice proper universal precautions throughout the specimen collection and handling process.
 - Wash Hands
 - Wear Gloves
 - Use biohazard disposal containers
- Ensure all tubes are labelled prior to sample draw
- Collect all serum samples prior to collecting anticoagulated samples to prevent the possibility of anticoagulant carryover.
- Collect full tubes of blood.
- Mix blood by gently inverting the tube eight times. Do not shake



Sample Processing

8mL SST Red and Yellow Top Tube – Chemistry, TSH, Total T3 and T4, IgE and Serum Pregnancy (not at Visit2), Visit 2 and Visit 7



- 1 - Draw 8mL SST tube
- 2 - Allow the tube to stand at room temperature for 30 minutes
- 3 - Centrifuge the tube at **1500g for 10 minutes**
- 4 - Remove the tube from the centrifuge after spinning and pipette **all** the serum (top clear layer) into **3 x** plain 3mL cryovial tubes
- 5 - Transfer the cryovial tubes into the bubble wrap bag ready for **ambient** shipment to ACM Global. Discard the SST tube.

Sample Processing (2)

5mL SST Red and Yellow Top Tube – Chemistry and Pregnancy, Visit 1. Chemistry, IgE and pregnancy, Visits 3, 4 ,5, 6 and 8



- 1 - Draw 5mL SST tube
- 2 - Allow the tube to stand at room temperature for 30 minutes
- 3 - Centrifuge the tube at **1500g for 10 minutes**
- 4 - Remove the tube from the centrifuge after spinning and pipette all the serum (top clear layer) into **2 x** plain 3mL cryovial tubes
- 5 - Transfer the cryovial tubes into the bubble wrap bag ready for **ambient** shipment to ACM Global. Discard the SST tube.

Sample Processing (3)

5ml SST Red and Yellow Top Tube – RAST Visits 1 and 7



- 1 - Draw 5mL SST tube
- 2 - Allow the tube to stand at room temperature for 30 minutes
- 3 - Centrifuge the tube at **1500g for 10 minutes**
- 4 - Remove the tube from the centrifuge after spinning and pipette all the serum (top clear layer) into **1 x plain 3mL cryovial tube**
- 5 - Transfer the cryovial tubes into the bubble wrap bag ready for **ambient** shipment to ACM Global. Discard the SST tube.

Sample Processing (4)

5ml SST Red and Yellow Top Tube – PD-1, Visits 2 -8 and Unscheduled



- 1 - Draw 5ml SST tube
- 2 - Place the SST tube on ice and perform sample processing within 30 minutes
- 3 - Centrifuge the tube **at 2000g for 10 minutes at 4°C**
- 4 - Remove the tube from the centrifuge after spinning and pipette **all** the serum (top clear layer) into 1 x plain 2mL cryovial tube. Discard the SST tube
- 5 - **FREEZE IMMEDIATELY** at –20°C until shipping

No Refrigerated Centrifuge?

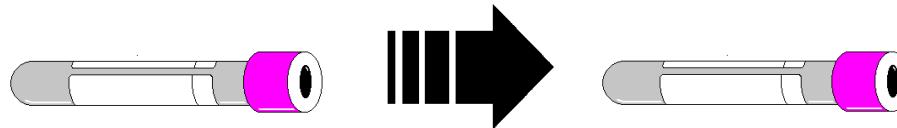
- Cool the element in the fridge, or fill the bucket with ice
- After blood draw and sample inversion, cool sample on ice
- Within 30 minutes, centrifuge sample at 2000g for 10 minutes in a centrifuge with pre-cooled elements.



AC-060A202: CONTROL – Central Laboratories
Investigators Meeting, Barcelona – 20 & 21 January 2011

Sample Processing (5)

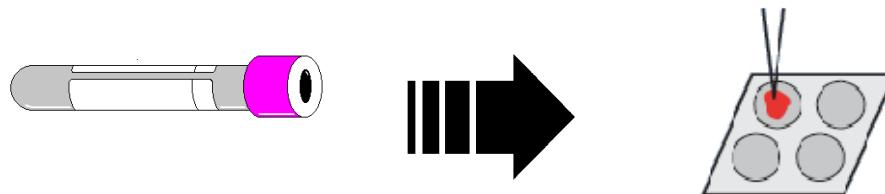
3mL EDTA Purple Top Tube – Haematology , All Visits



- 1 – Draw the EDTA tube
- 2 - Gently invert the tube for 10-15 seconds to ensure proper mixing of anticoagulant and blood
- 3 - Transfer the EDTA tube into the bubble wrap bag ready for **ambient** shipment to ACM Global

Sample Processing (6)

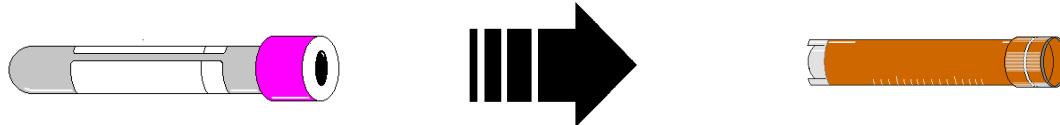
2mL EDTA Purple Top Tube and FTA Whatman Card – PD-3,
Visit 2



- 1 – Draw the 2mL EDTA tube
- 2 - Gently invert the tube for 10-15 seconds to ensure proper mixing of anticoagulant and blood
- 3 – Using the pipette provided place 1 drop of EDTA blood onto each circle of the FTA Whatman Card.
- 4 - Transfer the FTA Whatman Card into the bubble wrap bag ready for **ambient** shipment to ACM Global

Sample Processing (7)

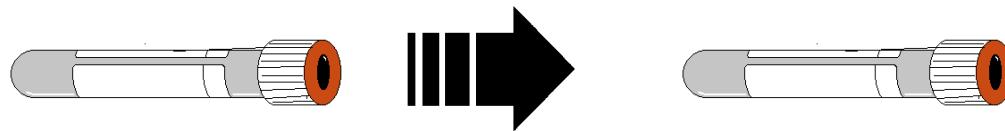
2ml EDTA Purple Top Tube – PK, Visits 3, 4, 5, 6, 7 and Unscheduled (Plus Visits 4 and 5 for PK-CM Sub-Study Patients)



- 1 – Draw the 2ml EDTA tube
- 2 - Gently invert the tube for 10-15 seconds to ensure proper mixing of anticoagulant and blood
- 3 – Place the EDTA tube on ice and perform sample processing within 30 minutes
- 4 - Centrifuge the tube at 2000g for 10 minutes at 4°C *
- 5 - Remove the tube from the centrifuge after spinning and pipette all the plasma (top clear layer) into 1 x 2mL amber cryovial provided at each draw
- 6 – **FREEZE IMMEDIATELY** at –20°C until shipping

Sample Processing (8)

2.5mL PAXgene Brown Top Tube – PD-2, Visits 2 and 7



- 1 – Draw the 2.5mL PAXgene tube ensuring the tube is completely filled
- 2 - Gently invert the tube for 10-15 seconds to ensure proper mixing of anticoagulant and blood
- 3 – Leave the PAXgene tube at room temperature for a minimum of 2 hours (maximum 24 hours) before transferring the tube to a – **20°C freezer. Store frozen until shipping**

Sample shipping – Ambient Samples

- Seal the 95 kPa bag containing sample tubes and the SUPASORB™ absorbent pad
- Place the sealed 95 kPa bag inside an assembled fibreboard box with a copy of the laboratory request form(s) and seal.
- Place the box inside a clear courier bag but do not seal. Sign and date a pre-printed courier Air Waybill and place into the document wallet of the courier bag
- The box should now be sent to ACM Global using the courier service as instructed in your laboratory manual



AC-060A202: CONTROL – Central Laboratories
Investigators Meeting, Barcelona – 20 & 21 January 2011

Sample shipping- frozen samples

- ACM Global will contact sites every 2 – 4 months to arrange a suitable collection date
- Please respond promptly to enable quick turn-around
- ACM Global will make all the arrangements with World Courier to collect all frozen samples
- Dry ice and all documentation will be provided by the courier
- Place samples and request form inside 95pka bag for transportation provided by courier
- Lay bag on top of dry ice and replace box lid
- Sign and date documentation as requested by courier



Data Cleaning

- Upon receipt at central laboratory, all samples are checked for data consistency between the sample tube/s and request form
- Inconsistencies noted in database
- Data Inconsistency Form faxed to investigator on same day as sample receipt
- Corrections made to database 'real-time' and report held until query is resolved

Laboratory Reports

- Laboratory reports will be issued by fax to investigators
- Reports will be emailed to investigators in cases of line problems
- Results viewed on ACM Global LabStar website – access for:
 - Actelion project team
 - Actelion research scientists
 - Region monitors and coordinators



Questions?

Global and Europe - ACM Global, York, UK

Stacey Fergusson, Project Manager Europe

Tel: +44 1904 699 411 Fax: +44 1904 699 401

E-mail: sfergusson@acmgloballab.co.uk



AC-060A202: CONTROL – Central Laboratories
Investigators Meeting, Barcelona – 20 & 21 January 2011